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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/729,920	12/06/2000	Karl Guegler	CL000858	7457

25748 7590 10/15/2003

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EXAMINER	
BASI, NIRMAL SINGH	

ART UNIT	PAPER NUMBER
1646	13

DATE MAILED: 10/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/729,920	GUEGLER ET AL.	
	Examiner	Art Unit	
	Basi N Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Amendment filed 5/2/03 (paper number 11) has been entered.

2. Sequence Listing filed 5/2/03 has been entered. The sequence listing in the CRF contained errors, i.e. contained non-ASCII "garbage" at the beginning/end of files. The errors in the CRF were corrected by the STIC Systems Branch. The non-ASCII "garbage" at the beginning/end of files was deleted.

3. Information Disclosure statement filed 12/19/02 (paper number 9) has been entered and considered.

4. The drawings filed 5/2/03 (paper number 10) have been entered. The drawings are approved by the examiner.

5. ***Sequence Rules Compliance***

This application still fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in Figure 1-3 must be identified by their corresponding SEQ ID NO:. Compliance with sequence rules is required. Peptide fragments in Figure 1A and 1B must be identified by SEQ ID NO:. All sequences in Figure 2A-D must be identified by SEQ ID NO:, Applicant has only identified SEQ ID NO:4 and 5 (there are more than two sequences disclosed in Figures 2A-D). Sequence in Figure 3 1B must be identified by SEQ ID NO:.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (12/2/02).

7. Response to Applicants Arguments for claim rejections under 35 USC § 101 and 35 USC § 112, 1st paragraph

Claims 4, 8-9 and 24-29 remain rejected under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph, for reasons of record in paper number 8 (12/2/02). Applicant argues molecules of the present invention have uses within the commercial market place in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets. Applicant also argues, the present invention provides sufficient knowledge and information that is beneficial to the public, provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/ or diagnostics, the disclosure of a new member of this family advances the art and augments the capabilities of biomedical researchers to combat illness, the claimed invention is a valuable drug target and has apparent commercial utilities such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers. Applicant further argues since TREK channels are highly expressed in anterior/preoptic hypothalamus they may be involved in neurodegeneration . Applicant also argues the nucleic acid of instant invention are commercially useful for developing therapeutic agents for treating diseases. Further applicant argues that membership to the family of potassium channels is sufficient to support for a substantial and specific use even though each member may play a somewhat different role in cellular responses. Applicant arguments have been fully considered but not found persuasive.

Neither the specification, nor the art of record, disclose the protein of SEQ ID NO:2 or polynucleotide of SEQ ID NO:1 and 3, which are useful to identify drugs that affect said protein and modulate its activity. Similarly, neither the specification nor the art of record disclose any

instances where disorders associated with claimed nucleic acid dysfunction can be effected by interfering with the activity of the protein of SEQ ID NO:2 or polynucleotide of SEQ ID NO: 1 and 3. Thus the corresponding asserted utilities are essentially methods of treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed nucleic acid, vector comprising said nucleic acid or cells comprising said vector, further experimentation is necessary to attribute a utility to the claimed invention. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). The specification (page 16) discloses, analysis of sequences the human genome was used to identify fragments encoding peptides that share structural and/or sequence homology to protein/peptide/domains identified or characterized in the art. Based on homology analysis applicant concluded, "the present invention provides amino acid sequences of human transporter peptides and proteins that are related to the potassium channel subfamily". The specification contains no experimental data disclosing that claimed invention encodes a protein that transports potassium. The ligands that bind/activate protein encoded by the nucleic acid of instant invention have not been disclosed. There is no disclosure of agonists or antagonists to claimed channel protein. The specification discloses the claimed

polynucleotide of claimed invention is expressed in wide variety of tissues. There is no clear nexus between the expression of claimed polynucleotide and a disease state or dysfunction. The invention further relates to methods using the receptor polypeptides and polynucleotides as a target for diagnosis and treatment in potassium channel-mediated disorders. In light of the specification the skilled artisan can speculate that the claimed invention may comprise a protein that belongs to potassium channel of proteins. However, no disclosure is provided within the instant specification on what specific function claimed ion channel possesses, or how to specifically assay for such, ligands that bind, promoters that activate, nor are any disease states disclosed that are directly related to dysfunction of claimed nucleic acid or its encoded protein thereby. Applicant argues that TREK2 may be up-regulated or down-regulated by neurotransmitter receptors and G-PCR. . The neurotransmitter and specific G-PCR that regulate claimed invention are not disclosed. There is no disclosure of which neurotransmitter/G-PCR would up-regulate , which would down-regulate. The effects of down-regulation or up-regulation are not disclosed. Is up-regulation beneficial or detrimental to the cell or disease state? Is down-regulation beneficial or detrimental to the cell or disease state? Is a disease state associated with up-regulation or down regulation. The specification and applicants arguments state that the claimed polynucleotides are useful as tools for drug discovery, screening assays and the diagnosis of disease. For a utility to be "well-established" it must be specific, substantial and credible. All nucleic acids and genes and their encoded polypeptides may in some combination be useful in drug discovery, screening assays and the diagnosis of disease. However, the particulars of testing with SEQ ID NO:1-3 are not disclosed in the instant specification. Neither the specific disease states, screening assays or ligands that bind to the protein encoded by

claimed invention are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO:1-3. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polynucleotide in an array for screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants' individual polynucleotide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this nucleic acid could be put.

With regard to diagnosis of disease, in order for a polynucleotide or protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in a wide variety of tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA or protein and the disease. If a molecule is to be used as a

surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of a clear disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The specification fails to disclose sufficient properties of the protein and/or polynucleotide (SEQ ID NO:1-3) to support an inference of utility. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases and telomerases share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. To argue that all the members can be used for screening/testing for drugs, and diagnosis of disease, producing antibodies, developing hybridization probes and primers is to argue a general, nonspecific utility that would apply to virtually every member of the family, contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

Without knowing a biological significance of the claimed polypeptides or the polynucleotides or the polypeptide encoded thereby, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by channel proteins. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient

likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The utility of claimed ion-channel cannot be implicated solely from homology to amino acid/nucleic acid sequences of channel proteins because the art does not provide teaching stating that all members of the potassium channel family must have the same effects, the same ligands and be involved in the same disease states. In instant application the inference of function of the polynucleotides of SEQ ID NO:1 and 3 is based on homology to potassium channels (no data is provided as to the %homology, only conclusion). There is no support in the specification nor prior art that the polynucleotide of SEQ ID NO: 1 and 3 encodes a functional protein, other subunits may be required for functionality.

Applicant asserts that the use of the claimed invention for drug discovery, screening assays and the diagnosis of disease are substantial utilities. The question at issue is whether or not the broad general assertion that the claimed nucleic acids might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might

be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

Even though, instant invention may have some sequence homology to potassium channel sub-family a reasonable correlation to its function and activity has not been established. The present rejection under § 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. As Applicant recognizes, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. Therefore, for reasons set forth above, and in paper number 8, the rejection under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph are maintained. The claimed invention is not supported by either a specific or substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
October 8, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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